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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1 to 22, 44, to 50 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1 to 22, 44 to 50 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☑ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

1) Claims 9 to 22 and 44 to 50 are pending in the instant application. Claims 1 to 8 and 23 to 43 have been canceled and claims 11, 44 and 50 have been amended as requested by Applicant in Paper Number 6, filed 23 December of 1996.

2) This application does not contain an Abstract of the Disclosure as required by 37 C.F.R. § 1.72(b). An Abstract on a separate sheet is required.

3) 37 C.F.R. § 1.84(U)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a **capital** letter. Figures 1a and 1b on the instant application, for example, should be renumbered 1A and 1B. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4) The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of a genomic DNA, nucleic acid which regulates the expression of a scavenger receptor protein or encodes a human scavenger receptor protein such that an artisan could make and use that nucleic acid. Further, because there is no description of the claimed nucleic acid it is not possible to determine if the instant claims encompass a compound that was disclosed by the art prior to the making of the instant invention. The only nucleic acids which are provided by the instant specification are three cDNAs whose nucleotide sequences are presented in SEQ ID NOs: 3, 5 and 7 of the instant application. There is absolutely no description in the instant specification of any genomic DNA or a nucleic acid which regulates the expression of a scavenger receptor protein. At best, the text on pages 38 and 39 of the instant specification identifies those methods through which nucleic acids which encode proteins having other than the three disclosed amino acid sequences might be obtained. Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016, held that;

> "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and describe how to obtain it. *See Oka*, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by

> its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated"

Claims 11 to 13, 16, 18 and 19 constitute nothing more than a wish to know the identity of any compound having the recited biological activity.

Claims 11 to 13, 16, 18 and 19 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

5) The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for the production of an antibody which "selectively" binds to a scavenger receptor protein of the instant invention. On of ordinary skill in the art would interpret the term "selectively" as requiring the claimed antibody to only bind to a scavenger receptor protein and to no other compound. To be able to produce an antibody with the required selectivity an artisan would have to know the complete amino acid sequence and tertiary structure of every protein which is encompassed by the term "scavenger receptor protein" as well as the complete amino acid sequences and tertiary structures of every other protein in the universe. Because this information is not in the instant specification or

the art of record and the acquisition of this information is currently beyond the skill of the artisan, that artisan can not make an antibody with the required specificity.

6) Claims 9 to 13, 15, 17 19 to 22 and 44 to 50 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is not enabling for the production of an isolated nucleic acid encoding a scavenger receptor protein lacking one of the amino acid sequences that are disclosed in SEQ ID NOs:4, 6 and 8 of the instant application. The text beginning on line 38 of page 38 of the instant specification states that the term " scavenger receptor BI" encompasses proteins comprising those amino acid sequences of SEQ ID NOs: 4 and 8 of the instant application "and degenerate variants thereof and their equivalents in other species of origin, especially humans, as well as functionally equivalent variants, having additions, deletions, and substitutions of either nucleotides or amino acids which do not significantly alter the functional activity of the protein as a receptor characterized by the binding activity identified above". It is unclear from reading the instant specification what the term "the binding activity identified above" is referring to. Because there is no limitation on the nature of the "additions, deletions, and substitutions" that can be made in the disclosed amino acid sequences or the sequences of "equivalent" proteins from other organisms, the instant claims

essentially encompass a nucleic acid encoding any protein which possesses the ability to bind low density lipoproteins, an antibody reactive thereto and a plurality of methods of using that protein. The recitation of the limitation "scavenger receptor protein which selectively binds to low density lipoprotein and to modified lipoprotein having the characteristics of acetylated low density lipoprotein" is nothing more than a recitation of a biological activity which places no structural limitations on the claimed composition. Because claim 11 places no structural limitation on the claimed composition it is, in essence, a single means claim because it encompasses any composition having a recited activity whereas the instant specification only discloses those three compositions known to the inventor. As determined in *In re Hyatt*, 218 USPQ 195 (CAFC 1983) such a claim does not meet the requirements of 35 U.S.C. § 112, first paragraph, because the instant specification does not disclose any and all compositions which meet the sole functional limitation of the claims.

In so far as these claims encompass a nucleic acid which encodes a scavenger receptor protein lacking one of the naturally occurring amino acid sequences that are disclosed in the instant application, an antibody to that protein or a method of using that protein, the instant specification does not identify those amino acid residues in the amino acid sequence of SEQ ID NO:4, 6

or 8 which are essential for the biological activity and structural integrity of a scavenger receptor protein and those residues which are either expendable or substitutable. In the absence of this information, working examples or the identification of analogous proteins for which this information is known a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 500 amino acid residues before they could even begin to rationally design a nucleic acid encoding a functional scavenger receptor protein having other than a natural amino acid sequence. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

An artisan can not alter the amino acid sequence of any of the three scavenger receptor proteins that are disclosed in the

instant specification by following the guidance provided therein and have "their performance characteristics predicted by resort to known scientific law". See M.P.E.P. §§ 706.03(n) and 706.03(z).

7) The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for a method of inhibiting the uptake of lipoprotein or lipids by selectively inhibiting the binding of those compounds to a scavenger receptor protein. The instant specification does identify a single compound which inhibits the uptake of lipoprotein or lipids by selectively inhibiting the binding of those compounds to a scavenger receptor protein nor does it provide a method of administering such a compound. To practice such a method would require a knowledge of the route, duration and quantity of administration of that protein to a subject and this information is not provided by the instant specification. The text on pages 43 to 54 of the instant specification clearly fails to supply the guidance that would be needed by a routine practitioner. The instant specification has also failed to disclose how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working example, prophetic or actual, of the claimed method. In the absence of this guidance a practitioner would have to resort to a substantial amount of

undue experimentation involving the variation in the amount and duration of administration of any experimental compound which is identified in accordance with the instant invention in determining a suitable protocol for administration. The instant situation is directly analogous to that which was addressed in In re Colianni, 195 U.S.P.Q. 150, C.A.F.C., which held that a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

Claim 49 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

8) Claims 44 to 50 are rejected under 35 U.S.C. § 112, first paragraph, because they are incomplete. Each of these claims is drawn to a method and yet none of them recite sufficient elements to provide the claimed method. Claim 44, for example, includes the step of "providing an assay for binding" which lacks any defining elements.

9) Claims 9 to 22 and 44 to 50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing

to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9.1) Claims 9 to 22 and 44 to 50 are vague and indefinite because it is not possible to identify that material which is encompassed by the term "scavenger receptor protein" from that material which is excluded by this term. The instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a scavenger receptor protein. In the absence of this information one can not determine the metes and bounds of a claim which relies upon this term as a limiting element.

9.2) Claim 9 is incorrect because there is no antecedent basis for "scavenger receptor protein". There is no single protein which is identified in either the art of record or the instant specification as "scavenger receptor protein". This claim should properly refer to "a scavenger receptor protein" since the instant specification indicates that a plurality of different proteins are encompassed by the term "scavenger receptor protein".

9.3) Claim 12 is incorrect because "lung" and "liver" are organs, not cells.

9.4) Claim 13 is incorrect because a nucleic acid "sequence, not being a material entity, is incapable of hybridizing to anything.

9.5) Claim 14 is vague and indefinite in the recitation of the term "or a degenerate variant thereof". Either the claimed nucleic acid encodes the amino acid sequence of SEQ ID NO:4 or it doesn't.

9.6) Claim 15 is vague and indefinite because an amino acid sequence can not "consist essentially of" an amino acid sequence. Either the first amino acid sequence "is" the reference sequence, "comprises" the reference sequence or is "comprised by" that sequence. The term "consist essentially of" is employed in the art to identify to critical components in a chemical composition. An amino acids sequence is not a component in a composition, it is a property of a compound and a compound either comprises that property or it doesn't.

9.7) Claim 19 is incorrect because there is no antecedent basis for "the" human scavenger receptor. Neither the art of record or the instant specification recognizes a single protein as "the" human scavenger receptor.

9.8) Claim 21 is incorrect because there is no antecedent basis for "encoding the scavenger receptor" in claim 11, which is not limited to a nucleic acid encoding a protein. This claim is also incorrect because an isolated nucleic acid can not "comprise" a vector, however, a vector can comprise an isolated nucleic acid.

9.9) Claim 22 is incorrect because a nucleic acid can not "comprise" a host cell.

9.10) Claim 45 is incorrect because a nucleic acid sequence is not a compound, it is a property of a compound.

9.11) Claims 45 to 47 are incorrect because there is no antecedent basis for "[t]he assay of claim 44", which is drawn to a "method for screening".

9.12) Claim 46 is confusing because the term "naturally occurring or synthetic compounds" implies that there is a third alternative.

9.13) Claim 47 is vague and indefinite because it does not identify the element whose binding to the receptor is being competitively inhibited by the compound.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

10) Claims 11 to 22 and 50 are rejected under 35 U.S.C. § 101 because they are drawn to nonstatutory subject matter.

10.1) Claims 11 to 22 are drawn to a nucleic acid sequence. A nucleic acid sequence is a property of a nucleic acid and not a material entity in and of itself. Properties such as sizes, shapes, colors and sequences are not subject to

patentability because a property is not a process, machine, manufacture, or composition of matter.

10:2) Claim 50 encompasses a process which comprising only mental steps. The step of determining and comparing can constitute nothing more than mental steps since a practitioner can "determine the presence" of a protein in a patient by reviewing test results.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11) Claims 11, 12, 15, 17, 19 and 20 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by the Calvo et al. publication (J. Biol. Chem. 268(25):18929-18935, 05 Sept. 1993). Figures 2 and 3 on pages 18931 and 18932 of the Calvo publication provided the nucleotide sequence of a recombinant DNA encoding a human protein that is identified therein as CLA-1 and the amino acid sequence of the protein encoded thereby. A comparison of the amino acid sequence of this protein with SEQ ID NO:4 of the instant specification clearly shows that CLA-1 is the human homolog of the hamster type BI scavenger receptor protein of the instant invention. The amino acid sequence of CLA-1 is identical to SEQ ID NO: 4, both of which are 509 amino acids in length, in

414 residues out of those 509 residues. Additionally, these sequences contain 62 conservative amino acid residues. Only 33 of the 509 residues in these two sequences do not match. These proteins are clearly species homologs of the same protein and both are encompassed by the term "scavenger receptor protein type BI" as defined in the instant specification. The labeled nucleic acid of claim 20 can be found in Figure 5 on page 18933 of this reference.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

12) Claims 9, 10, 13, 14, 18, 19, 21 and 22 are rejected under 35 U.S.C. § 103 as being unpatentable over the Calvo et al. publication (J. Biol. Chem. 268(25):18929-18935, 05 Sept. 1993). The text in the sixth and seventh full paragraphs on page 18932 of the Calvo et al. publication disclosed that CLA-1 belonged to the same protein family and was structurally analogous to a protein identified therein as LIMPII. Figure 1A on page 18930 of the Calvo et al. publication demonstrated that the amino acid sequences of the rat and human LIMPII proteins were highly conserved between these mammalian species. The text in the last paragraph on page 18930 and the first paragraph on page 18931 of Calvo et al. demonstrated that the nucleotide sequences of the genes encoding rat and human LIMPII were of sufficient similarity to permit the isolation of a DNA encoding human LIMPII by using DNA primers from DNA encoding rat LIMPII. An artisan would have reasonably concluded, based upon the experimental evidence present in the Calvo et al. publication, that a DNA encoding any mammalian CLA-1 protein could be readily isolated by probing an appropriate DNA library with a probe corresponding to a DNA encoding the human CLA-1 that was described in Figures 2 and 3 therein. Because the hamster, in addition to the rat, mouse and guinea pig, was routinely employed as a laboratory model for determining the physiological significance of proteins of human origin since the scope of human experimentation is obviously

limited, an artisan of ordinary skill would have found the production of hamster CLA-1 by isolating a DNA encoding the hamster homolog of the human CLA-1 described by Calvo et al. to determine the physiological significance of that protein to have been prima facie obvious at the time that the instant invention was made. Because Calvo et al. had presented evidence that the sequences of the genes and the proteins that are encoded thereby which are members of the CLA-1, LIMPII, CD36 gene family are conserved between different mammalian species and particularly between humans and rodents, an artisan had more that a reasonable expectation that a DNA encoding the hamster homolog of CLA-1 could have been isolated by screening a hamster DNA library with a human CLA-1 DNA probe.

The text in the seventh and eighth full paragraphs on page 18930 of the Calvo et al. publication shows that the expression of a recombinant DNA like that which was described in Figures 2 and 3 of Calvo et al. to obtain the isolated protein encoded thereby in quantity and to permit the characterization of that protein at the molecular level was routine in the art at the time of the instant invention. An artisan of ordinary skill, therefore, would have found it prima facie obvious to have produced the CLA-1 protein of Calvo et al. by incorporating the cDNA described therein into an expression vector and heterologous host by employing those methods which were routine in the art at

the time that the instant invention was made to permit the quantitative production of CLA-1 and to facilitate its characterization at the molecular level.

Claims 9 and 10 encompass an antibody which "specifically" binds to the CLA-1 protein of Calvo et al. While neither the instant specification or the art of record are enabling for this limitation, an antibody which binds to a scavenger receptor protein would have been *prima facie* obvious since the production of antibodies to recombinantly produced proteins to permit the immunological detection of those proteins in a sample was a routine practice in the art of molecular biology at the time of the instant invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm at telephone number (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM. The fax phone number for this group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.t

JOHN ULM
PRIMARY EXAMINER
GROUP 1800